



Practice-changing abstracts selected
by the GvHD Hub Steering Committee

61st ASH Annual Meeting & Exposition
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The **world-leading experts** in graft-versus-host disease (GvHD) shared the top abstracts from ASH 2019 that they believe could have the **greatest impact on clinical practice**.

In this document, you will find comments from the GvHD Hub Steering Committee members on GvHD and microbiome, predicting GvHD before transplantation, the role of post-transplant cyclophosphamide to prevent GvHD, and the role of conditioning to reduce GvHD.

GvHD and microbiome

#194: Impact of Gut Mycobiota Composition on Outcomes after Allogeneic Hematopoietic Cell Transplantation



Professor Mohamad Mohty

“Fungal diversity in patients receiving allo SCT is low, however predominance of *Candida* correlates with poor survival. In addition, specific gut bacteria were found to have an effect on patient outcome, and therefore broad spectrum antibiotic use and oral intake diversity could have an effect on survival.”

[what-s-new-in-microbiota-research-on-the-outcomes-after-allogeneic-hematopoietic-stem-cell-transplantation](#)



Professor Takanori Teshima

“Malard *et al.* from Hospital Saint Antoine, Paris, showed fungal microbiota also play a role; *Candida* colonization is associated with higher incidence of acute GvHD and mortality. This study links to our recent basic study showing that *Candida* augment Th17 alloresponses (Uryu, Blood 2015) and a recent study from Paris (Legoff, Nat. Med. 2017) showing gut virome is also associated with transplant outcome. However, there are many open questions to be addressed before practice changing.”



Doctor Zinaida Peric

“Malard *et al.* showed that patients undergoing allo-HSCT have a low fungal diversity at the day of transplant as well. Namely, they presented the results of a study conducted in 52 patients undergoing allo-HSCT confirming the disruption of fungal microbiota in these patients. They also showed that the increased amount of *Candida albicans* and *Malassezia genera* at the time of allo-HSCT independently predicts mortality, while patients colonized with higher amount of *Candida glabrata* have a higher incidence of grade II–IV acute GvHD. All these findings together raise the interest of possible interventions for the restoration of gut microbiota which could improve the outcome of allo-HSCT patients.”

GvHD and microbiome

#597: Antibiotic Exposures and Dietary Intakes Are Associated with Changes in Microbiota Compositions in Allogeneic Hematopoietic Stem Cell Transplant Patients



Professor Takanori Teshima

“Nguyen *et al.* from Memorial Sloan Kettering showed that type of antibiotics and type of dietary intakes are associated with changes in microbiota composition after allo-SCT. Since dysbiosis is associated with transplant outcome, microbiota stewardship clinical practice may improve transplant outcome, as oral care and physical rehabilitation do.”



Doctor Zinaida Peric

“Nguyen *et al.* have also presented at ASH the results of a large microbiota study in over one thousand allo-HSCT patients and demonstrated the association of various antibiotic exposures with different changes in microbiota composition. More precisely, using a regression-based approach that predicts cluster transitions in response to antibiotics, they found that pip-tazo exposure was associated with destabilization of a high-diversity state and increased transitions to a *Streptococcus*-dominated state, while cefepime and meropenem exposure did not disrupt high-diversity microbial community. Furthermore, this study group analysed dietary habits of their patients and found that increased protein intake is associated with disruption to the high-diversity cluster, while increased fat intake strengthened the maintenance of a diverse and healthy microbial community.”

[what-s-new-in-microbiota-research-on-the-outcomes-after-allogeneic-hematopoietic-stem-cell-transplantation](#)

Predicting GvHD before transplantation

#48: Genetic Alterations at Diagnosis Predict Outcome of AML Patients Age 60 or Older Undergoing Allogeneic Transplantation in First Remission



Doctor Ali Bazarbachi

“Murdock *et al.* from Dana Farber Cancer Institute identified, in older patients with AML allografted in CR1, those with low genetic risk and remarkably good outcomes, and those with very high-risk genetics who have limited benefit from current transplant approaches. This is very important given the recent major increase in transplant activity in older patients.”



Professor Attilio Olivieri

“This interesting study focuses on the impact of genetic signature in 252 elderly patients with AML and builds a predictive model capable of convincingly stratifying patients and their outcome, based on these signatures. These results are extremely important and come from a multicenter study in the US, thus laying the foundations for a possible change in clinical practice in this setting.”

[molecular-profiling-at-diagnosis-for-risk-stratification-of-patients-with-aml-undergoing-allogeneic-transplant-in-first-remission](#)

#39: Pre-Transplant Serum Claudin-3 Predicts Intestinal Graft-Versus-Host Disease and Non-Relapse Mortality Risk after Allogeneic Hematopoietic Cell Transplantation



Professor Attilio Olivieri

“This study of over 500 patients transplanted in the recent era suggests that the only biological marker statistically associated with a significant risk of acute intestinal GvHD (GI) is represented by claudin-3, a major component of the endothelium-epithelial narrow junction. The OR of developing acute GI GvHD in patients with elevated levels of claudin-3 was 1.16, while none of the other potential biological markers of acute GI GvHD proved significant. However interesting and however original the statistical methodology is, these results require large-scale prospective validation and therefore cannot yet be considered such as to be able to change clinical practice in the immediate future.”



Professor Florent Malard

“Gastro-intestinal acute GvHD is one of the most severe, life-threatening complications after alloHCT. The authors identify pre-transplant serum claudin-3 as a biomarker of gastro-intestinal acute GvHD and NRM. Upon validation on an additional cohort, identification of patients at increased risk of gastro-intestinal acute GvHD can be helpful in order to reinforce GvHD prophylaxis, for example.”

[pre-transplant-serum-levels-of-claudin-3-as-a-predictive-biomarker-for-intestinal-gvhd-and-non-relapse-mortality-risk-after-allogeneic-transplantation](#)

Role of post-transplant cyclophosphamide to prevent GvHD

#876: From Ex-Vivo T-Cell Depletion to Post-Transplant Cyclophosphamide: Improved GvHD-Free & Relapse-Free Survival but Comparable Chronic GvHD Incidence in Haploidentical Transplantation. A 15 Years EBMT Registry Analysis on Behalf of the TCWP-EBMT



Professor Attilio Olivieri

“This large retrospective study shows that the PTCy platform is characterized by a significant advantage both in terms of NRM, OS, and GRFS compared to the other T-depletion platforms used in the haploidentical setting. Furthermore, the comparison between the different sources of HSC suggests that the use of PBSC is characterized by a greater risk of extended cGvHD. As far as a retrospective study is concerned, the sample size and statistical significance strongly support the possibility that these results may modify clinical practice in the future.”



Professor Florent Malard

“This registry study performed by the Transplant Complication Working Party of the EBMT evaluates more than 3,000 patients transplanted with a haplo donor between 2004 and 2016. They find that development of the PTCy platform translates in an improved GvHD-free relapse-free survival. Nevertheless, chronic GvHD remains comparable and is still a major issue after alloHCT.”

[novel-prophylactic-therapies-available-before-and-after-transplantation-to-reduce-the-risk-of-gvhd](#)

[how-to-select-the-optimal-gvhd-prophylaxis-regimen](#)

Role of conditioning to reduce GvHD

#256: Myeloablative Fractionated Busulfan Conditioning Regimen in Older Patients: Results of a Phase II Study



Professor Attilio Olivieri

“This phase 2 study is certainly very interesting, both for the innovative approach and for the extremely good results in terms of reduced NRM and outcome. However, the limited number of patients and the need to confirm the results in a larger population, and possibly in a multicenter manner, are factors that prevent us from being able to judge it as a study that will change practice.”

#255: Reduced Risk of Relapse for Total Body Irradiation + Fludarabine Compared to Busulphan + Fludarabine As “Reduced-Toxicity” Conditioning for Patients with Acute Myeloid Leukemia Treated with Allohsct in First Complete Remission. a Study By the Acute Leukemia Working Party of the EBMT



Professor Arnon Nagler

“This is a very important abstract because a reduction in GvHD toxicity is seen similar to that achieved by reduced intensity conditioning, and this could be practice-changing in transplantation.”

[novel-prophylactic-therapies-available-before-and-after-transplantation-to-reduce-the-risk-of-gvhd](#)

[the-comparison-of-reduced-intensity-stem-cell-transplantation-conditioning-regimens-in-patients-with-high-risk-aml](#)

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